

**Amendments to the Drawings:**

The attached sheet of drawings includes changes to Fig. 1. This sheet replaces all prior versions of Fig. 1. The replacement sheet makes the following corrections:

- (1) the cobalt center in the porphyrin ring has a charge of “+” instead of “+3”;
- (2) the Ring A carbon that is bonded to Ring D has a methyl, not hydrogen, substituent;
- (3) the nitrogen atom in Ring D forms a double and not single bond with the ring carbon to its left, thus the hydrogen bonded to that double-bonded carbon is deleted; and
- (4) the Ring D nitrogen atom forms a dative and not covalent bond with the cobalt center; and
- (5) the dimethylbenzylimidazole has a “+” charge on its top nitrogen atom and a covalent instead of dative bond to cobalt.

Attachment: Replacement Sheet

Annotated Sheet Showing Changes

## **REMARKS/ARGUMENTS**

Claims 1-3, 5-8, and 11-31 remain in the application. Claims 1, 5, 7-8, 11-18, 20-21, and 28 have been amended, without prejudice or disclaimer of any previously claimed subject matter. Claims 4, 9, and 10 are cancelled. Claims 29-31 are new.

Figure 1 has been amended to correct some inadvertent typographical errors as noted on page 25 herein. Amended Figure 1 conforms with the known structure of vitamin B12. As stated on page 7, lines 28-29, “The structure of various forms of vitamin B<sub>12</sub> is shown in **Figure 1**, wherein X is CN, OH, CH<sub>3</sub> or 5'-deoxyadenosyl, respectively.” The specification refers on page 7, line 32 to the Vitamin B<sub>12</sub> ring system depicted in The Merck Index, Merck & Co., 11<sup>th</sup> ed. (1989) (a copy of which is enclosed as Appendix A). Also enclosed as Exhibit B is a copy of The Merck Index, Merck & Co., 12<sup>th</sup> ed. (1996) which also depicts vitamin B12. Formula (I) also is amended in the specification on pages 13 and 31 and in claims 1 and 18 to correct an inadvertent typographical error in the charge on the Co(III) atom, which should be “+”, consistent with Vitamin B<sub>12</sub> in The Merck Index, Merck & Co. 11<sup>th</sup> ed. (1989), page 1577.

## **Specification**

The Examiner objected to the embedded hyperlink at page 3, lines 13-14 of the specification under MPEP § 608.01. The hyperlink has been deleted in the amendment herein.

## **Claims**

The Examiner objected to the semicolon in Claim 4. Claim 4 is canceled.

The Examiner objected to multiple dependent claims 12-14 depending from other multiple dependent claims. The improper multiple dependency is corrected in the current amendment.

## **Rejections Under 35 U.S.C. § 112**

Claim 1 is rejected as being unclear. To promote prosecution, claims 1 and 18 have been amended to remove arrows and labels as noted by the Examiner.

Claim 1 is rejected because of parenthetical phrases. Currently amended claims 1 and 18 to remove the parentheses.

Claim 1 is rejected for reciting a “singular molecular weight”. The specification

describes a linker of “unimodal (i.e., single) and defined molecular weight.” See page 12, lines 16-21, and page 23, lines 27-32 of the present application. To promote prosecution, currently amended claims 1 and 20 recite “unimodal” instead of “singular”.

Claim 1 is also rejected for reciting “significantly impaired”. Claims 1 and 18 have been amended to recite that the compound displays a binding affinity to a transcobalamin receptor of “at least 50% of the binding affinity displayed by vitamin B<sub>12</sub>”. See page 31, lines 1-3 of the specification.

The Examiner rejected claim 1 on the grounds that Y, R, G, E, K, M, and V require numerical indicators. Currently amended claim 1 now recites these indicators.

The Examiner rejected claim 5, for lack of clarity. To promote prosecution, amended claim 5 recites a poly(amino acid) residue comprising one or more T, consistent with the specification (see page 45).

#### **Rejections Under 35 U.S.C. § 102(e)**

The Examiner rejected claim 1 under 35 USC § 102(e) on grounds of anticipation by Russell-Jones et al. (US 6,262,253), which discloses a vitamin B<sub>12</sub> analogue linked to GCSF or EPO. This rejection is traversed to the extent it is applied to the amended claims.

Russell-Jones et al. does not identically disclose the subject matter of the amended claims. Russell-Jones et al. does not disclose a compound as recited in the claims, wherein the linker comprises a natural amino acid, in D- or L- form, an unnatural amino acid or a peptide, as recited in independent amended claim 1. Russell-Jones et al. also does not disclose the compounds recited in new claim 31 wherein Z<sup>2</sup> is L-T.

Further, Russell-Jones et al. teaches conjugates for *oral* delivery: “The present invention relates to the oral delivery of the therapeutic substances granulocyte-colony stimulating factor (GCSF) and erythropoietin (EPO) by administration of a complex comprising these substance linked to vitamin B12 (VB12) or an analogue thereof,” col. 1, l. 11-15). By contrast the present application discloses *non-oral* administration: “It is preferred that the TC- or IF-binding carrier and the therapeutic and/or diagnostic agent be administered parenterally and not orally to increase the effectiveness of the agent, for example, in the case of imaging, to decrease the exposure of normal cells to the diagnostic agent.” See page 19, l. 29-32 of the current application. Currently amended independent claim 18 is directed to parenteral, intrathecal,

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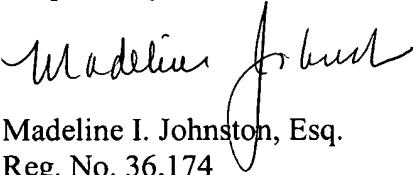
topical, vaginal, nasal spray, or surgical implant administration.

Accordingly withdrawal of this rejection is requested.

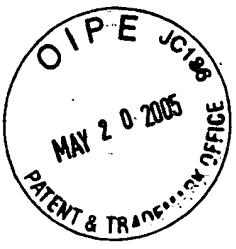
## CONCLUSION

In view of the above arguments, and amendments to the claims, Applicant respectfully requests allowance of the pending claims. Please charge any fees not included herewith, associated with this filing, or credit any overpayment, to Deposit Account No. 11-0980.

Respectfully submitted,

  
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Date: May 16, 2005  
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**CERTIFICATE OF MAILING (37 CFR 1.8a)**

I hereby certify that this Amendment and Response to Non-Final Office Action, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450.

Jennifer A. Williams

A handwritten signature in black ink, appearing to read "Jennifer A. Williams", is written over a single horizontal line.

May 16, 2005

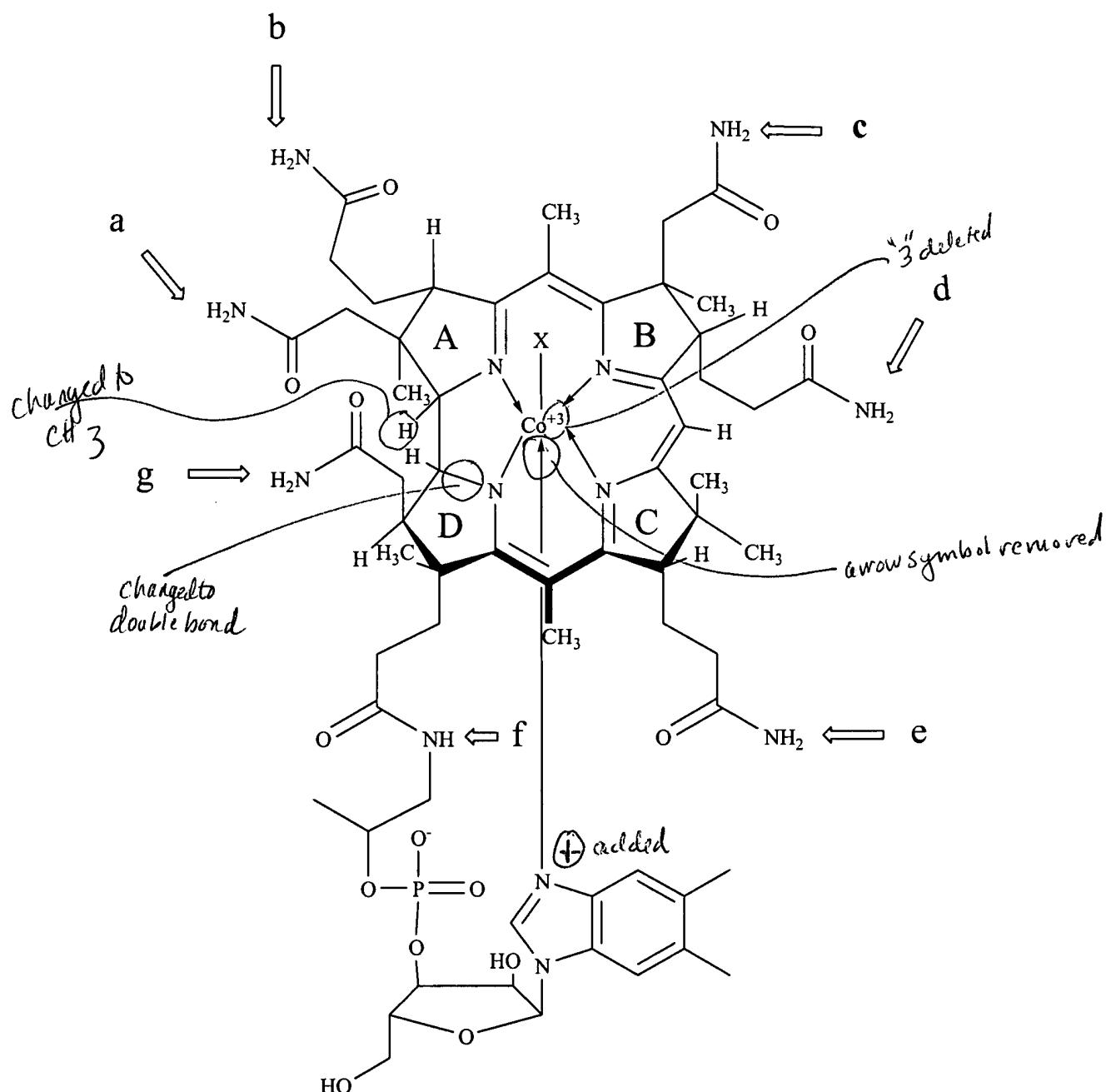


FIGURE 1